REMARKS

Claims 1-9 and 16-19 were pending in the application and were rejected. Claims 1, 9, 14-16, and 18-19 were amended herein and claims 2-8 were canceled herein, all without prejudice and without acquiescence, and solely to further prosecution of the case; support for the amendments is at least in the original claims. Applicants reserve the right to pursue amended material in subsequent prosecution.

Claims 10-15 and 26 were entered and withdrawn herein, pursuant to the Examiner's admission on pages 3-4 of the Office Action mailed August 10, 2007, that Groups I and II and I and V were related as combination and subcombination, and that claims found allowable in Group I would apply to Groups II and V. In a teleconference of January 18, 2008, the Examiner confirmed the suitability of re-entering but withdrawing these claims for possible rejoinder in later prosecution. No new matter is entered herein.

I. 35 USC § 112 First Paragraph (Enablement)

Claims 1-9, 16, and 18-19 were rejected under 35 USC § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to enabled the skilled artisan how to make and use the invention.

The Examiner has suggested that undue experimentation would be required to treat diseases in which cell division is already too low. In view of this rejection, and in order to advance the prosecution of this application, claim 1 is now focused upon disorders in which increased cell division occurs. This amendment is believed to overcome the Examiner's rejection.

Applicants respectfully request withdrawal of the rejection.

II. 35 USC § 112 Second Paragraph

Claims 4-5, 7, 9, 16, and 19 were rejected under 35 USC § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter of the invention.

Claims 4, 5 and 7 are now cancelled. The Examiner's rejection is therefore rendered moot.

The relevant SEQ ID numbers have been introduced into claims 9 and 16 as requested by the Examiner. The relevant SEQ ID numbers have also been introduced into withdrawn claims 14 and 15.

A clarifying amendment has been made in claims 18 and 19 to refer to the cells in which increased cell division occurs. It is therefore believed to be clear that these cells are the same ones in which increased cell division occurs in the disorder of claim 1.

III. 35 USC § 103 Obviousness

Claim 1 is rejected under 35 USC § 103 as being unpatentable separately over Lillie (U.S. 2003/0124128; "Lillie"); Lorens (U.S. 2004/0053233; "Lorens"); and Rubenfield (U.S. Patent No. 6,551,795; "Rubenfield").

Although Applicants respectfully disagree that claim 1 is unpatentable over these documents, claim 1 is amended herein solely to further the prosecution of this case, and therefore the claims are clearly distinguished from that in the prior art documents cited by the Examiner.

The Lillie and Lorens documents cited by the Examiner both disclose amino acid sequences comprising the sequence FPWMKEKKS. This partial sequence does not meet the requirements of claim 1. For example, claim 1 now explicitly requires that the amino acid at position X2 is tyrosine (Y). Neither of the sequences disclosed in Lillie or Lorens includes a tyrosine residue at a suitable position. Similarly, the sequence referred to by the Examiner in the Rubenfield patent (WDWMSRRRRLS) is not a sequence as required by claim 1 presently on file.

None of the documents cited by the Examiner thus discloses a peptide comprising an amino acid sequence as recited in claim 1. Furthermore, none of these documents suggests that or gives an apparent reason why such a peptide might have utility in the treatment of a disorder in which increased cell division occurs. The peptide sequences cited by the Examiner from each of these three documents are in fact only small fragments of much larger sequences. There is nothing in any of these documents that indicates that these particular regions might be of importance in the treatment of disorders involving increased cell division. There is nothing in these documents that would teach the skilled reader to try to make changes within these small regions of the disclosed polypeptides, and nothing that would encourage the skilled reader to

make the amino acid changes that would be necessary in order to achieve a peptide as defined in claim 1.

Furthermore, the present inventors have demonstrated that peptides as defined in the claims are particularly active. In particular, the specific peptide referred to in the specification as HXP or HXP4 is shown to have improved activity when compared to the control peptide CXP or CXP4.

The consensus sequence now recited in claim 1 incorporates the HXP4 peptide and excludes the CXP4 peptide. The consensus sequence recited in claim 1 also incorporates some other peptide sequences that are related to HXP4. The consensus sequence in claim 1 was derived by the inventor based on additional experimental data and his expert knowledge in this field enabling him to predict which substitutions of which amino acids at which positions in this sequence would still lead to an effective peptide.

Annex I herewith shows further experimental data obtained using exemplary variant peptides. The peptides used in Annex I all consist of a peptide having a sequence X1 to X7 and further comprising a cell penetration moiety wherein the cell penetration moiety is either a penetratin sequence (RQIKIWFQNRRMKWKK) or a polyarginine penetration sequence consisting of 9 arginine residues (R9).

The data presented in Annex I shows the IC50 values for a number of peptides in murine B16F10 melanoma cells. These include the HXP4 peptide discussed in detail in the present application, which has an IC50 of 19, and the CXP4 control peptide used in many of the Examples of the present application, which has a much higher IC50 value of 61. It can be seen from Annex I that the peptide comprising the same X1 to X7 peptide as HXP4, but including the R9 penetration sequence rather than the penetratin sequence, has a very similar IC50 value to the HXP4 peptide. Similarly, some amino acid substitutions within this sequence, particularly to the amino acids X4 to X7, also led to peptides having low IC50 values. However, other substitutions within this core sequence led to significant increases in the IC50, including unallowable substitutions at positions X2 and X3 and substitutions of the W and M residues specified in the consensus sequence of claim 1.

Based on this experimental data, together with their common general knowledge in this field, the inventors have derived the consensus sequence recited in claim 1, and it is believed to

be reasonable to predict that substantially all peptides falling within that consensus sequence would have the claimed technical effect.

The present invention is therefore based upon the surprising discovery of a small group of peptides that mimic the region of HOX to which PBX binds and which act as an antagonist of that binding. As demonstrated in the present application, such peptides have been found to have cross-reactivity and reduce the binding of PBX to all HOX proteins. The data presented in the present application and in Annex I as attached show that the group of peptides specified in the claims is a small and specific group of peptides that have a demonstrable effect. This particular group of peptides and the effects that they are able to achieve would not have been deduced by the skilled reader of any of the prior art documents referred to by the Examiner. It is therefore submitted that the claimed subject matter is not obvious.

IV. Conclusion

In view of the amendments now made and the arguments presented herein, favorable reconsideration of the application is respectfully requested.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 06-2375, under Order No. HO-P03185US0.

Dated: June 13, 2008

Respectfully submitted,

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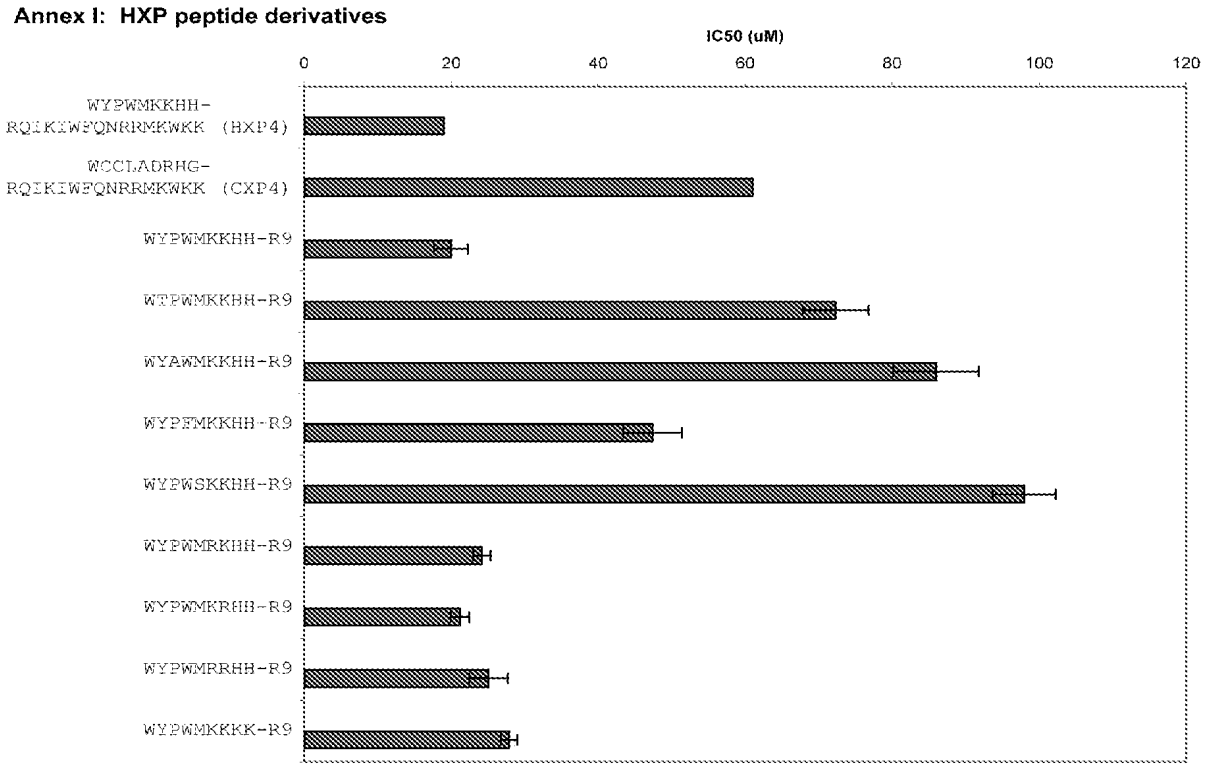
ANNEX 1


Annex I: HXP peptide derivatives
IC50 (uM)
0
20
40
60
80
100
120
WYPWMKKHH-RQIKIWFQNRRMKWKK (HXP4)
WCCLADRHG-RQIKIWFQNRRMKWKK (CXP4)
WYPWMKKHH-R9
WTPWMKKHH-R9
WYAWMKKHH-R9
WYPFMKKHH-R9
WYPWSKKHH-R9
WYPWMRKHH-R9
WYPWMKRHH-R9
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